PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 03 AUG 2005
WIPO PCT

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
JWJ01051WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/003880	10.09.2004	12.09.2003

International Patent Classification (IPC) or national classification and IPC
C07K14/025, C12N5/10

Applicant
RENEURON LIMITED et al.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
01.04.2005	02.08.2005

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/003880

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-35	as originally filed
Claims, Numbers	
1-26	as originally filed
Drawings, Sheets	
1/7-7/7	as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/003880

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-26
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-26
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-26
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Present application is based on the finding that T antigen binds to Bub1 protein kinase, and that this interaction is responsible for the genomic instability sometimes associated with T antigen expressing cells. However, said interaction is not required for immortalisation of cells and so disrupting this binding is useful for the preparation of genetically stable immortalised cell lines. A SV40 T antigen protein that lacks the ability to bind the Bub1 protein, polynucleotides encoding said proteins as well as recombinant mammalian cells comprising said polynucleotides and therapeutic uses thereof are claimed.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 The following documents were taken into account:

D1: WO 01/21790 A (RENEURON LIMITED; LUDWIG INSTITUTE FOR CANCER RESEARCH) 29 March 2001 (2001-03-29)

D2: ROBERTS ET AL: "THE SACCHAROMYCES CEREVISIAE CHECKPOINT GENE BUB1 ENCODES A NOVEL PROTEIN KINASE" MOLECULAR AND CELLULAR BIOLOGY, WASHINGTON, DC, US, vol. 14, no. 12, December 1994 (1994-12), pages 8282-8291, XP002084403 ISSN: 0270-7306

V.2 Novelty (Article 33(1) and (2) PCT)

The available prior art documents neither disclose a SV40 T antigen that lacks the ability to bind to the Bub1 protein nor refer to recombinant cells comprising a polynucleotide encoding a T antigen that is modified to prevent the binding between the T antigen and Bub1. Hence, the subject matter of claims 1 - 26 is not anticipated by the available prior art and therefore it complies with the requirements of Article 33(1) and (2) PCT.

V.3 Inventive Step (Article 33(1) and (3) PCT)

D1 which is considered to represent the closest prior art refers to the immortalisation of cells based on the use of a conditionally-inducible oncogene (such as the ts SV40 T antigen) in combination with the catalytic subunit of the telomerase complex (hTERT). In particular, the use of the double SV40 mutant U19tsA58 is disclosed.

The present application differs from D1 in that a SV40 T antigen mutant that lacks the ability to bind to the Bub1 protein is used in order to immortalise mammalian cells.

The problem to be solved by the present application can therefore be considered as the provision of further mutant SV40 T antigen protein and its use in order to immortalise

cells.
The solution provided by the present application is the SV40 T antigen mutant that lacks Bub1 binding.
The subject-matter of D2 concerns the characterization of the Bub1 gene. However, it neither refers to an interaction of the Bub1 protein with the T antigen nor to the relevance of said interaction with regard to chromosomal stability.
Hence, the subject-matter of claims 1 - 26 is considered to be inventive under Article 33(3) PCT: none of the available prior art documents contains any disclosure that could alone, or in combination with other cited documents suggest the invention of the current application.

V.4 Industrial Applicability (Article 33(1) and (4) PCT)

The subject matter of claims 1 - 26 is considered industrially applicable. Hence, it meets requirements of Article 33(1) and (4) PCT.

Re Item VIII

Certain observations on the international application

1) *Claims 24 - 26 are not adequately supported by the description. Said claims are directed to the use of a cell according to any of claims 11 - 23 in the manufacture of a medicament for the treatment of disorders such as Alzheimer's disease or Parkinson's disease. However, so far the present application does not disclose any data showing a medical use of the claimed cells with regard to a specific disease. Hence, the subject-matter referred to in said claims is purely speculative and said claims are not considered to fulfill the requirements of Article 5 and 6 PCT.*